Reviewed By
RAAOUM M. JABOR

Thromboembolic Disease

Objectives:

- → List the predisposing factors for thromboembolism in pregnancy.
- → Discuss the clinical presentation and management of superficial thrombophlebitis.
- → Discuss the clinical presentation and management of deep vein thrombosis.
- → Discuss the clinical presentation and management of pulmonary embolism in pregnancy.

- → Explained Slides
- → Department's Slides (Dr. Maha)
- → Important
- → Golden notes
- → Extra
- → Doctor's notes
- → Previous Doctor's notes
- → Reference

Kaplan Video

Editing File

Thromboembolic Disease

Venous Thromboembolic Disease (TED):

- → Serious and important disease.
- → **Effect:** one of the major causes of **direct maternal deaths**, survivors suffer significant **morbidity**.
- → **Incidence:**
  - → 2 - 4x up to 5x ↑ compared to non-pregnant state.
  - → Overall low.
  - → **US:** 1 in 500 - 2000 pregnancies (**absolute incidence:** 0.025 - 0.1%).
- → **Prevalence:** 1 in 1600.
- → **Risk factors:**
  - → Cesarean delivery > vaginal delivery.
    - → ↑ infections risk & endothelial injury to uteroplacental & pelvic vessels in emergency c-section → ↑ risk of TED.
    - → All 3 elements of Virchow triad (stasis - endothelial injury - hypercoagulability) are present → predispose pregnant woman to VTE.
  - → Pregnancy period.
    - → **Pathophysiology:**
      - → Pregnancy → changes in coagulation factors (↓ protein S & antithrombin + ↑ fibrinogen, factors V, VI, VII, VIII and X + von Willebrand factor) → favor clotting (*hypercoagulable state*).
      - → Gravid uterus compresses pelvic veins + endocrine-mediated vasodilation → venous stasis often aggravated by ↓ mobility.
    - → **Result:**
      - → An isolated lower extremity DVT.
      - → Clot break off from lower extremities & travel to lung to present → PE.
  - → Puerperium (postpartum) period.
    - → Compared with antepartum period: VTE is 2 - 5x more common.
    - → Highest risk in the first 6 weeks postpartum, declines to general population by about 13 - 18 weeks.
- → **Symptoms:**
  - → Overlap with pregnancy symptoms → may impair clinical suspicion → challenging diagnosis.

1. Deep Vein Thrombosis (DVT):

- → **Incidence:**
  - → 75% occur **antepartum** (equal in 3 trimesters).
  - → 25% postpartum → consider DVT risk after delivery especially cesarean section.
- → Detection of DVT during pregnancy is critical to preventing deaths from PE.

2. Pulmonary Embolism (PE):

- → **Incidence:**
  - → 2 / 100 000 pregnancies.
  - → 40 - 60% occur **postpartum** during the first few weeks (first 2 & up to 6 weeks).
    - → 80% of cases are left-sided → give prophylactic **heparin** post cesarean section.
- → Major **non-obstetric** cause of maternal mortality.
  - → **Hemorrhage:** major **obstetric** cause of maternal mortality
- → 7th leading cause of maternal mortality.
- → Responsible for 9 % of maternal deaths.
- → **Fatality rate:** 15% (high) especially in the 1st hour.

Thromboembolic Disease

Why Pregnancy is Associated with ↑ Clotting Tendency?

→ Changes happen to minimize postpartum hemorrhage, but could lead to clotting.

Strongest predisposing risk factor:
Compression of uterus on inferior vena cava + pelvic veins → **venous stasis** → slow venous return.

Hypercoagulable State "↑ clotting tendency":
- ↓ **anticoagulants:** protein S + antithrombin
- ↑ fibrinogen + factors V, VI, VII, VIII & X + von Willebrand factor.

↑ plasminogen activator inhibitor → ↓ fibrinolytic activity.

Endothelial damage during pregnancy and delivery to uteroplacental and pelvic vessels.

Risk Factors:

→ Highlighted risk factors → antepartum, from Dr. Maha's slides.

↑ maternal age:
≥ 35 years
Make pt aware of risks

Inflammatory bowel disease

Obesity:
- > 80 kg
- **AP:** BMI ≥ 30 kg/m^2
- **PP:** BMI ≥ 25 kg/m^2

Eclampsia or preeclampsia

Varicose veins

Immobility
medical or non medical, prescribed bed rest for certain obstetric complications

Urinary tract infection

Multiparity / multiple births:
≥ 4 births

Diabetes

Operative delivery
Emergency C-section > elective

Atrial fibrillation
No heart compression (stasis)

Personal / family history of TED (DVT / PE)

Previous history:
- IUFD
- Early PET
- Severe IUGR
- Abruption.

Pelvic/leg trauma:
- During current pregnancy or previous trauma.
- Especially fractures.

Smoking

Hypertension

Stillbirth

Obstetric hemorrhage

Young gestational age
Preterm delivery <36 weeks

Cardiac disease

Acquired or inherited thrombophilia:
- Antithrombin deficiency.
- Factor V Leiden.
- protein C deficiency.
- protein S deficiency.
- Recurrent pregnancy loss → acquired / congenital

Antiphospholipid antibodies + **lupus** anticoagulant → usually **recurrent abortions** & intrauterine fetal death.

Hospitalization for non-delivery reasons (*particularly those >3 days***)**

Postpartum infection

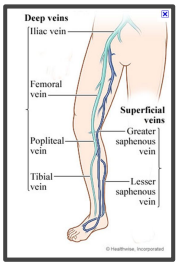
Blood Transfusion

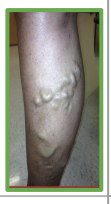
Non Specified | Antepartum | Both | Postpartum

1. Venous Thrombosis

Types of Venous Thrombosis:

	Superficial Thrombophlebitis	Calf Deep Vein Thrombosis (below knee)	Proximal/ilio-femoral Deep Vein Thrombosis

General	→ Commonest form of venous thrombosis in pregnancy & puerperium.
	→ In 1% of patients.
	→ **More common in:**
	  → Varicose veins (*nearly always arise in existing varicose veins*).
	  → Progress to superficial thrombophlebitis, very rare for superficial thrombophlebitis to happen without an existing varicose veins.
	  → Obesity.
	  → Limited physical activity.
	  → Previous history of superficial thrombosis.
	  → Nearly always arise in existing varicose veins
	→ Misnamed condition.
	  → Not infective, redness surrounding the affected vein is a reaction to clot.
	→ Usually does not progress to DVT or lead to PE.
		→ Most (75 - 80%) resolve spontaneously → run a benign course depending on the size and patient's history (*e.g. history of thrombophilia*) and risk factors.
		→ Sometimes (20 - 25%) the thrombus spreads up to involve proximal deep veins → 50% risk of pulmonary embolism.
		→ Unlike superficial thrombophlebitis, DVT does predispose to thromboembolic disease.
			→ Occurs more commonly than CVT.
			→ Over 80% is left-sided due to compression of left iliac vein by the overlying right iliac artery.
			→ More proximal → more serious.
			→ More involvement of deep veins → more serious.
			→ 70% of DVT in pregnancy.
			→ Unlike superficial thrombophlebitis, DVT does predispose to thromboembolic disease.
			 

Clinical Presentation	→ Mostly limited to calf area. → Swelling of involved extremity. → Tenderness of involved extremity. → Erythema & redness. → Palpable cord-like veins over the course of involved superficial vein. → Warmth. → **Diagnosis:** calf superficial thrombophlebitis, might come in **OSCE**! 	→ Pain. → Local tenderness. → Swelling. → Change in skin colour. → Change in skin temperature. → Unilateral (left).	→ Pain → Symptoms are more dramatic. → المريضة تجي على عكاز → **Homan sign:** calf pain on foot dorsiflexion. → Swelling involving entire limb. → Unimpaired arterial supply → leg appears swollen, **blue** (venous, less oxygenated) **& warm** (more common). → If arterial spasm occurs secondary to irritation from nearby clotted vein → leg becomes swollen, painful, **white & cold** (more serious) → better prognosis.

Investigation	→ **Diagnosis:** clinically obvious
	→ In some patients, DVT need to be excluded as it may coexist with it.
	  → ↑ pain.
	→ concern of deep vein extension → lower-limb US.
	  → Rarely occurs especially when symptoms change.
		Discussed next slide	

Treatment	**Symptomatic:** → Compression bandage. → Support stockings → help avoid a repeat episode. → Leg elevation. → Encourage mobility & ambulation. → Pain medications. → Local application of heat. → Usually no anticoagulants. → Anti Inflammatory agents may be considered. → Follow up so it doesn't progress to ulceration and education.	*Discussed next slide*	

1. Venous Thrombosis

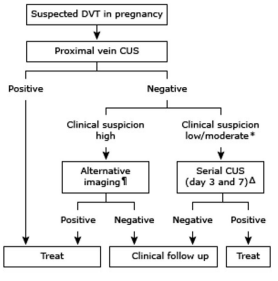
Clinical Features:

→ Clinical diagnosis of DVT is difficult and inaccurate in over 60% of cases of TED.
  → **Why?** leg symptoms (**oedema and pain**) and **dyspnea** are common in pregnancy and mimic symptoms of DVT/PE → we always have to assess the risk factors.
  → Tachycardia may be a normal physiologic response.
→ 50% of cases are asymptomatic.
→ **Homans sign:** pain in the calf in associated with dorsiflexion of the foot → thrombosis in calf veins.
→ Dull ache / tingling / tightness / pain in the calf or leg especially when walking.
→ Acute swelling & pain in thigh + tenderness in femoral triangle → suggestive iliofemoral thrombosis.
→ DVT in pregnancy is usually in the **left** leg.
→ Left lower-extremity pain & swelling + finding of a 2-cm difference in calf circumference → one of the more reliable clinical signs of a DVT in pregnancy.
→ **Indications for testing:** *one of them*
  → History of VTE.
  → First-degree relative with high-risk thrombophilia.
  → VTE age < 50 years.

Diagnosis:

→ **Contrast venography:** contrast in the leg veins (local vein), rarely used & diagnosis is rarely made by the demonstration of a filling defect in contrast.
→ **Duplex ultrasonography:** measure the flow, more commonly used with a sensitivity and specificity of 97%.
→ **Compressive ultrasonography (CUS):** noninvasive technique that has high sensitivity and specificity and is currently the **primary mode of diagnosis used for DVT**, more commonly used.
→ **Magnetic resonance imaging (MRI):** sensitivity and specificity 100% in non-pregnant patients, rarely used.
  → **Q:** is MRI one of the investigations? Yes, it has been used to evaluate patients suspected of having pelvic thrombosis who have a negative doppler ultrasonic examination.
  → Can be used to look for pelvic clot.
  → Magnetic resonance venography (MRV) is rarely used & diagnosis is rarely made by the demonstration of a filling defect in MRV.
→ **Pelvic vein ultrasound:** can be used to look for pelvic clot.
→ **CT scan:** can be used to look for pelvic clot, but not usually used because of radiation.
→ **D-Dimer:** not useful/reliable screening tool for VTE in pregnancy.
  → **Why?** because it normally ↑ with gestational age (**OSCE Q**).
→ **DVT diagnosis during pregnancy:**
  → Demonstrate lack of/poor compressibility of proximal veins on **compressive ultrasonography** (*femoral vein thrombosis*).
  → Poor flow on **Doppler** imaging of the femoral-iliac vein (*iliac vein thrombosis*).
→ **Successful DVT diagnosis in pregnancy and puerperium:** high index of clinical suspicion + low threshold for use of objective confirmatory testing.
→ **Wells score:** Wells and modified Wells scoring systems
  → Most commonly used scoring systems for nonpregnant patients with suspected DVT.
  → **Not validated** for use in pregnancy and should be interpreted with caution in this population.
→ D-dimer levels and clinical exam cannot be used alone to diagnose DVT.

Diagnostic algorithm for suspected deep venous thrombosis in pregnancy



DVT: deep vein thrombosis; CUS: compression ultrasound.

* Refers to patients with an initial negative CUS in whom clinical suspicion remains that is not high. Refer to UpToDate topics on DVT in pregnancy.

¶ Alternative imaging techniques include doppler ultrasound of the iliac vein and contrast or magnetic resonance venography.

Δ Consideration can be given to measuring a D-dimer level using enzyme linked immunosorbent assay (ELISA) or red blood cell agglutination (SimpliRED). A D-dimer level <500 ng/mL is considered negative and no further testing is needed. A D-dimer level >500 ng/mL is not diagnostic and has no value in directing further testing in pregnant patients.

UpToDate®

1. Venous Thrombosis

Treatment:

Heparin: *Start for acute PET!*

- → **Anticoagulant of choice** in pregnancy.
- → Standard **IV heparin** or the more preferred LMWH S.C. (**Trade name:** Clexane) should be started once the diagnosis is clinically **suspected** (even if not confirmed) until excluded by objective testing.
- → Both forms are don't cross placenta → safe for the fetus.
- → Breastfeeding is not a contraindication of heparin.
- → Can be reversed by **protamine sulphate** (antidote).
- → **Pregnant → initiated with heparin:** *either of the two options* → full anticoagulation but **start IV!**.
  - → **Intravenous unfractionated heparin (IV UFH):** 1.5 - 2.5 x control aPTT for at least 5 - 7 days then converted to S.C. continued for pregnancy duration + up to 6 weeks postpartum.
    - → Weekly monitoring of **aPTT**.
    - → Prolonged → higher risk of maternal thrombocytopenia + osteoporosis → monitor platelet count + follow up with hematologist → LMWH is better.
    - → Stopped 6 hours before delivery.
  - → **Subcutaneous low-molecular-weight heparin (S.C. LMWH - enoxaparin sodium):** 1 mg/kg subcutaneously every 12 hours.
    - → More effective and safer.
    - → Stopped 24 hours before delivery if planned induction or cesarean, or switch to UFH.

  - → حتى لو الاعراض اختفت اكمل العلاج بعد الولادة نحول إلى ورافرين.
- → Normal aPTT → safe administration of neuraxial anesthesia.

Warfarin:

- → **Warfarin:** a vitamin K antagonist.
  - → Crosses the placenta.
  - → Risks of fetal hemorrhage.
  - → Risks of teratogenesis.
  - → Breastfeeding is not a contraindication.
  - → Should be used only in the postpartum period.
    - → No signs of hemorrhage **postpartum** → LMWH or UFH can be restarted 12 - 24 hours post delivery then patient transitioned to warfarin for **at least 6 weeks** postpartum.
- → **International normalized ratio (INR):** used to measure effects of warfarin.
  - → **Target INR:** 2.5.
  - → **Range:** 2.0 - 3.0.

Other Treatments:

- → Elevate legs daily → reduce oedema.
- → Wear graduated elastic compression stocking daily → reduce oedema.
- → Measure calf circumference daily → monitors response to treatment.
- → Thoracotomy with embolectomy may be life saving if heparin did not work.

- → **Treatment aims:** aPTT = 2 - 2.5 for 5 - 7 days then continue with prophylactic dose generally for 6 -12 weeks post-nataly (not less the 6 weeks).
  - → حتى لو الاعراض اختفت اكمل العلاج بعد الولادة نحول إلى ورافرين.
- → **Optimal length of therapy/anticoagulation:** unknown & individualized.
- → **Total duration of anticoagulant therapy (pregnancy + postpartum):** at least 3 - 6 months for females whose only risk factors for VTE were transient (pregnancy - cesarean section).

- → Heparin thromboprophylaxis has to be considered in the subsequent pregnancies or if additional risk factors appear

I see you.. Its heparin dear .. HEPARIN

2. Pulmonary Embolism

Introduction:

→ A high index of suspicion is always needed for the diagnosis of PE especially in patients with DVT or risk factors for VTE.
→ One of the most common causes of pregnancy-related death in the United States.
  → **Maternal mortality:** < 1% if treated early, > 80% if left untreated.
    → **Maternal mortality rate with no treatment:** 13%, majority within 1 hour of the event.
    → **Survival rate with early diagnosis & treatment:** 92-95%
→ **70% of cases:** DVT is the instigating factor.
  → Early detection & treatment of DVT + widespread recognition of conditions or circumstances requiring DVT prophylaxis → ↓ PE incidence in pregnancy.

Clinical Features:

→ Signs and symptoms are nonspecific + mostly no prior clinical evidence of DVT (تتداخل مع أعراض الحمل).
→ In most obstetric patients, the signs and symptoms of a PE are subtle.

Symptoms				Signs
Tachypnoea	**Dyspnoea** *Shortness Of Breath*	Haemoptysis	**Pleuritic Chest Pain**	Air Hunger
Tachycardia	Cyanosis	Pyrexia *Low-Grade Fever*	Syncope or Varying Degree of Shock	Palpitations
Pleural Friction Rub	Chest Splinting	Pulmonary Rales	Accentuated Pulmonic Valve S2 Sound + Right Ventricular Failure	

2. Pulmonary Embolism

Diagnosis:

Routine	Diagnosis
→ **Chest X- ray:** commonly used, use abdominal shielding for protection, often normal. → **Chest film:** atelectasis, pleural effusion, obliteration of arterial shadows, and diaphragm elevation may be present. → **ECG:** commonly used, show sinus tachycardia with or without premature heartbeats or right ventricular axis deviation. → **Arterial blood gases:** commonly used, may show oxygen tension below 80 mm Hg, ↓ pO_2, but often in normal range.	***Used to locate the site of the clot*** → **Three algorithms may be used:** → **Bilateral compression ultrasonography of lower extremities (Compression Duplex Doppler):** commonly used to exclude DVT, positive for DVT → PE assumed in a symptomatic patient. → **Ventilation-perfusion lung scan (V/Q):** minimal risk to fetus, but can't be used in abnormal chest X-ray, asthma, or COPD. → **Computed tomographic (CT) pulmonary angiography:** noninvasive visualization of a thrombus (advantage). → Acceptably low radiation dose to fetus, but maternal breast tissue radiation exposure concern. → **Spiral CT scan:** superior to V/Q scan. → Best initial test for suspected PE. → **Most common indication:** a negative spiral CT scan in a high-risk and symptomatic patient. → **Arteriography:** if needed only, most definitive & diagnostic.

Treatment:

→ The acute treatment of PE and follow-up during pregnancy, labor, delivery, and the postpartum period are the same as for DVT.
→ **Treatment aims:** aPTT = 2 - 2.5 for 5 - 7 days then continue with prophylactic dose generally for 4 - 6 months post-nataly.
→ Massive PE → ICU & multidisciplinary team approach.
→ Recurrent PE (rare) → require inferior vena cava filter (a small device that can stop blood clots from going up into the lungs, common in oncology).
→ **Thrombolytic therapy:** only given with haematologist agreement.
→ **Streptokinase (plasminogen activator):** class C
→ **FDA Classification C:** animal studies have shown an adverse effect/risk on the fetus & there are no good studies in humans, but potential benefits may warrant use of the drug despite potential risks.

Thrombophilia Evaluation

Thrombophilia Evaluation:

- → **Considered for patients with a PE or DVT, especially:**
  - → Recurrent thrombosis.
  - → Positive family history.
  - → Obstetric history suggestive of antiphospholipid syndrome.
- → **Tests to order:**
  - → **Acquired thrombophilias:** lupus anticoagulant - anticardiolipin antibody.
  - → **Inherited thrombophilias:** factor V Leiden - prothrombin G20210A mutations - proteins C and S - antithrombin III titers.

Prophylactic Anticoagulant Therapy

Prophylactic Anticoagulant Therapy:

- → Prophylactic doses of heparin or LMWH should be given during pregnancy & 6 weeks postpartum.
  - → **S.C. injections of heparin:** 5000 - 10,000 U every 12 hours.
  - → **Enoxaparin sodium:** 40 mg once daily.
- → Mostly provide sufficient prophylaxis, some women may require full anticoagulation.
- → Planning for cesarean delivery → pneumatic compression stockings placed for thromboprophylaxis.

Oral Anticoagulants

Oral Anticoagulants:

- → Cross placenta → potentially teratogenic at any stage of pregnancy.
  - → That's why history taking is important.
  - → نوقف الوارفرين قبل التخطيط للحمل عشان لا تحمل و هي ما وقفت الدواء
- → Safe **after** delivery.
- → Safe for lactation.

Warfarin Teratogenicity (Fetal Warfarin Syndrome): describe the features:

- → Nasal hypoplasia.
- → Depressed nasal bridge → saddle nose.
- → Irregular bone growth → growth retardation.
- → Intracranial fetal haemorrhage.
- → Defects of limbs, eyes, and central nervous system.

Other agents:

- → **Rivaroxaban (Anti-factor Xa inhibitor):** class C
  - → **FDA Classification C:** animal studies have shown an adverse effect/risk on the fetus & there are no good studies in humans, but potential benefits may warrant use of the drug despite potential risks.

Risk of Radiologic Procedures to the Fetus:

- → **Radiation exposure of up to 0.05 Gy (5 rad) in utero:**
  - → **Oncogenicity:**
    - → Relative risks: 1.2 - 2.4
    - → Absolute risk of malignancy (baseline) in fetus: 0.1%.
  - → **Teratogenicity:**
    - → No increase in pregnancy loss, growth or mental retardation.

Conclusion:

- → Thromboembolism is a major cause of maternal mortality & morbidity worldwide
- → Clinical diagnosis is unreliable but once strongly suspected, treatment should be started until objectively excluded.
- → **Main diagnostic tools during pregnancy:** duplex doppler - x-ray venogram - V/Q scan.
- → LMWH is the preferred anticoagulant as it is more effective and safer than standard heparin.
- → Oral anticoagulants should not be given at any stage during pregnancy but they are safe & may be more convenient after delivery.
- → High clinical suspicion with early full anticoagulation and objective diagnosis are the best ways to minimize maternal mortality & morbidity and avoiding risks of the unnecessary treatment

439 Summary

Thromboembolic disease

Overview:

- 75% of DVT occur antepartum
- 43-60% of PE occurs postpartum (first 2-weeks post delivery).
  - PE is the major **non-obstetric cause** of maternal mortality.
  - Hemorrhage is the major **obstetric cause** of maternal mortality.

Risk factors of DVT:

Any factor that causes hypercoagulability, endothelial damage, and/or venous stasis can cause DVT

Transient risk factor	Chronic risk factor

• Surgical factor:
  ○ Surgery under GA, C-section
• Immobilization
  ○ Acute illness requiring complete bed rest
  ○ Pelvic or leg trauma
• Estrogen-related
  ○ Pregnancy
  ○ Use of OCP or hormonal replacement therapy
  ○ Multiparity (≥4)
• Patient factors
  ○ **Obesity**
  ○ Smoking
	• Patient factors
	  ○ Age > 35
	  ○ Personal Hx of DVT or PE
	  ○ Family Hx of DVT or PE
	• Thrombophilias
	  ○ Antiphospholipid syndrome (causes abortion in 1st trimester)
	  ○ Antithrombin deficiency
	  ○ Factor V Leiden, protein C, protein S deficiency

Others: infections, atrial fibrillation, previous hx of: IUFD/ severe IUGR/ Abruption/ Preeclampsia/ SLE	

Types:

	Superficial Thrombophlebitis	Calf DVT (CVT)	Proximal/ Iliofemoral DVT	Pulmonary Embolism (PE)
Overview	• Commonest form of venous thrombosis in pregnancy and puerperium • Nearly always arise in existing **varicose veins**, obesity, limited physical activity • **Does not predispose to thromboembolism,** but may mimic more severe disease	• Most common • Most resolve spontaneously except when the thrombus spreads up to involve the proximal deep veins in which case there is a 50% chance of PE • **DVT predisposes to thromboembolism**		Potentially fatal result of DVT
Clinical Features	Tenderness, erythema, palpable cord-like veins	• There may be no complaints • Pain, local tenderness, increased skin sensitivity, change in skin color and temperature, calf pain on foot dorsiflexion (homan's sign)		Sudden onset severe chest pain & dyspnea, tachypnea, cyanosis, hemoptysis
Diagnosis	DVT might have to be excluded (as it may coexist with it)	• **Duplex ultrasonography:** sensitive & specific • Compression ultrasonography • Pelvic vein ultrasound, CT scan and MRI are all tests that can be used to look for pelvic clots • D-dimer: not useful, because it normally increases gestational age		• **V/Q scan:** most accurate noninvasive method in pregnancy • CXR is normal • Spiral CT: best initial • Angiography: most sensitive
Management	• Compression bandages & leg elevation • Bed rest, pain medications, local application of heat, anti-inflammatory agents may be considered. • Encourage mobility when symptoms disappear.	• Before treatment, obtain baseline CBC including: platelets and aPTT Treatment: • IV heparin (LMWH or Unfractionated) to increase PTT by 1.5-2.5 times the control value. Osteoporosis & thrombocytopenia are complications of prolonged heparin treatment. Therefore platelet count should be monitored regularly. • Once therapeutic levels are reached, SC heparin is used once • Heparin antidote: protamine sulfate • **Warfarin is contraindicated = teratogenic** (craniofacial & limb defects) Prevention/prophylaxis: • **Low molecular weight heparin**		

Quiz

Question 1:

→ **Which of the following patients has the highest risk for DVT?**

A. Primigravida
B. 33 year old
C. Vaginal delivery
D. Smoker

Question 2:

→ **What is the best initial test for detecting PE?**

A. X-ray
B. Spiral CT
C. Duplex doppler
D. V/Q lung scan

Question 3:

→ **A patient was diagnosed with DVT during pregnancy and was prescribed LMWH injections , after delivery she asked if she can switch to an oral drug instead of injections. How will you proceed?**

A. Switch to oral warfarin
B. Discontinue anticoagulants after delivery
C. Switch to oral heparin
D. Do nothing

Question 4:

→ **Which one of the following is a useless test during pregnancy?**

A. V/Q lung scan
B. Duplex Doppler
C. D -dimer
D. X-ray

Question 5:

→ **A 32 year old pregnant female presented to your clinic complaining of tenderness and erythema over her leg. You suspect thrombophlebitis, how will you manage the patient?**

A. Low molecular weight heparin subcutaneously
B. Warfarin orally
C. Leg elevation and compression bandage
D. Admit and monitor patient

1	2	3	4	5
D	B	A	C	C

Reference

Venous Thromboembolic Disorders

Pregnancy is a hypercoagulable state with up to a fivefold increased risk of deep vein thrombosis (DVT) and pulmonary embolism (PE). **The greatest risk of a venous thromboembolism (VTE) is during the first few weeks postpartum,** especially following a cesarean delivery. Pregnancy-induced changes in coagulation factors that favor clotting include a decrease in protein S and increases in fibrinogen; factors VI, VII, and X; and von Willebrand factor. Venous stasis results from compression of the pelvic veins by the gravid uterus, as well as endocrine-mediated venodilation, often aggravated by decreased mobility. Delivery, especially an operative delivery, can cause endothelial injury to uteroplacental and pelvic vessels. Thus, all three elements of the Virchow triad (stasis, endothelial injury, and hypercoagulability) are present and predispose the pregnant woman to VTE. **Additional important risk factors are previous history of a DVT or PE, acquired or inherited thrombophilias, smoking, and prolonged immobility** as a result of prescribed bed rest for certain obstetric complications.

DEEP VEIN THROMBOSIS

Clinical Features

The clinical diagnosis of DVT is difficult. **Fifty percent of cases are asymptomatic.** Pain in the calf in association with dorsiflexion of the foot **(positive Homans sign)** is a clinical sign of thrombosis in the calf veins. Dull ache, tingling, tightness, or pain in the calf or leg, especially when walking, may be present. Acute swelling and pain in the thigh area, as well as tenderness in the femoral triangle, are suggestive of iliofemoral thrombosis. **DVT in pregnancy is usually in the left leg.** In a patient complaining of left lower-extremity pain and swelling, the finding of a 2-cm difference in calf circumference is one of the more reliable clinical signs of a DVT in pregnancy.

Investigations

Compression ultrasonography is a noninvasive technique that has high sensitivity and specificity and **is currently the primary mode of diagnosis** used for **DVT. Magnetic resonance imaging** (MRI) has been used to evaluate patients suspected of having pelvic thrombosis who have a negative Doppler ultrasonic examination. **D-Dimers** are not a reliable screening tool for VTE in pregnancy.

Therapy

Treatment of proven DVT during pregnancy should be initiated with either intravenous unfractionated heparin or subcutaneous low-molecular-weight heparin (enoxaparin sodium) to achieve full anticoagulation. The unfractionated heparin dose is adjusted to 1.5 to 2.5 times the control aPTT. Intravenous anticoagulation should be maintained for at least 5 to 7 days, after which treatment is converted to subcutaneous heparin that must be continued for the duration of the pregnancy and for up to 6 weeks postpartum, with weekly monitoring of the aPTT. **Alternatively, enoxaparin can be administered at a dose of 1 mg/kg subcutaneously every 12 hours.** The dose can be adjusted to achieve anti–factor X levels of 0.6 to 1 U/mL. **Both forms of heparin are safe for the fetus and do not cross the placenta. Unfractionated heparin is associated with a higher risk of maternal thrombocytopenia and osteoporosis than is low-molecular-weight heparin.** Supplemental calcium and vitamin D_3 (2000 IU/day) should be advised, along with periodic platelet counts. Because of its longer half-life and the increased risk of spinal hematomas with neuraxial anesthesia, **low-molecular-weight heparin should be stopped about 24 hours before delivery in the case of a planned induction or cesarean delivery. Alternatively, the patient can be switched to unfractionated heparin that can be stopped 6 hours before delivery.** If the aPTT is normal, neuraxial anesthesia can safely be administered. If there are no signs of hemorrhage postpartum, low-molecular-weight or unfractionated heparin can be restarted 12 to 24 hours postdelivery and the patient can then be transitioned to warfarin, which should be continued for at least 6 weeks postpartum. **Warfarin is a vitamin K antagonist that crosses the placenta, carries risks of fetal hemorrhage and teratogenesis, and, with few exceptions, should be used only in the postpartum period.** The international normalized ratio (INR) is commonly used to measure the effects of warfarin, and the target INR is 2.5 (range: 2.0 to 3.0). **Breastfeeding is not a contraindication to the use of warfarin, low-molecular-weight heparin, or unfractionated heparin.**

PULMONARY EMBOLISM

PE is one of the most common causes of pregnancy-related death in the United States. The maternal mortality is less than 1% if treated early and greater than 80% if left untreated. In about 70% of cases, DVT is the instigating factor. Early detection and treatment of DVT and widespread recognition of conditions or circumstances requiring DVT prophylaxis are expected to decrease the incidence of PE in pregnancy.

Clinical Features

Suggestive symptoms of PE include pleuritic chest pain, shortness of breath, air hunger, palpitations, hemoptysis, and syncopal episodes. Suggestive signs of PE include tachypnea, tachycardia, low-grade fever, a pleural friction rub, chest splinting, pulmonary rales, an accentuated pulmonic valve second heart sound, and even right ventricular failure. **In most obstetric patients, the signs and symptoms of a PE are subtle.**

Investigations

An ECG can show sinus tachycardia with or without premature heartbeats or right ventricular axis deviation. On a chest film, atelectasis, pleural effusion, obliteration of arterial shadows, and elevation of the diaphragm may be present. Arterial blood gases obtained on room air may show an oxygen tension below 80 mm Hg. **PE is ultimately a radiologic diagnosis. Three algorithms may be used. (1) Bilateral compression ultrasonography of the lower extremities: If positive for DVT, a PE may be assumed in a symptomatic patient. (2) A ventilation-perfusion scan:** This method poses minimal risk to the fetus, but it cannot be used in patients with an abnormal chest X-ray or in patients with asthma or chronic obstructive pulmonary disease. **(3) Computed tomographic pulmonary angiography:** This technique has the advantage of noninvasive visualization of a thrombus. The radiation dose to the fetus is considered acceptably low, but there is concern about the radiation exposure to maternal breast tissue.

The acute treatment of PE and follow-up during pregnancy, labor, delivery, and the postpartum period are the same as for DVT.

Thrombophilia Evaluation

A thrombophilia workup should be considered for patients with a PE or DVT, especially those with recurrent thromboses, a positive family history, or an obstetric history suggestive of antiphospholipid syndrome. Tests to order include those for acquired thrombophilias (e.g., lupus anticoagulant, anticardiolipin antibody) and inherited thrombophilias (factor V Leiden and the prothrombin G20210A mutations, as well as proteins C and S and antithrombin III titers).

Prophylactic Anticoagulant Therapy

In pregnant patients with a past history of a PE or DVT, prophylactic doses of heparin or low-molecular-weight heparin should be given during pregnancy and continued for 6 weeks postpartum. **Subcutaneous injections of a prophylactic dose of heparin (5000 to 10,000 U every 12 hours) or enoxaparin sodium (40 mg once daily)** provide sufficient prophylaxis for most patients, although some pregnant women may require full anticoagulation. All pregnant women having cesarean delivery should have pneumatic compression stockings placed for thromboprophylaxis.

SUPERFICIAL THROMBOPHLEBITIS

Superficial thrombophlebitis is more common in patients with varicose veins, obesity, limited physical activity, or a previous history of superficial thrombosis. **In most patients, superficial thrombophlebitis is limited to the calf area, and symptoms include swelling and tenderness of the involved extremity.** Physical examination reveals erythema, tenderness, warmth, and a palpable cord over the course of the involved superficial veins. **Superficial thrombophlebitis usually does not progress to DVT or lead to PE,** but lower-limb ultrasound is indicated if there is concern that the thrombosis may extend into the deep veins.

Treatment

Treatment of superficial thrombophlebitis involves elevation of the leg, pain medications, and local application of heat. **There is usually no need for anticoagulants, but antiinflammatory agents may be considered.** Ambulation is encouraged, and patients should be **instructed to wear support stockings** to help avoid a repeat episode.

Med 441 Team:

Leader:

Sarah Alhamlan

Members:

Ghada Alharbi

Good Luck!

Med 438 Team:

Leaders:

Ateen Almutairi - Lama ALzamil

Members:

Sarah Alarifi – Deema Almaziad
Joud Alkhalifah

Med 439 Team:

Leader:

Bushra Alotaibi

Members:

Leena Almazyad - Mayasem Alhazmi